Genomic instability at recombinase signal sequences in the CS Alu element. Shen, M.R., Wilcox, D.A., Mohrenweiser, H.W., Biology and Biotechnology Research Program, L-452, Lawrence Livermore National Laboratory, Livermore, CA 94550.

Chromosomal rearrangements in some lymphocytic leukemias have been found to be mediated by V(D)J recombinase. Recombinase signal sequence (RSS) like sequences have been found in many of the pretranslocation break-points. This suggests that V(D)J recombinase may be a factor in the cause of lymphocytic leukemias. The CS Alu element contains a sequence that is very similar to both of the consensus RSSs. This CS Alu element represents 40,000 members per haploid genome. We show that the concensus CS Alu element inserted into the pJH299 recombinase vector is a substrate for V(D)J recombinase. This CS Alu element is able to act as both types of RSSs. The signal and coding junctions (products of V(D)J recombinase mediated rearrangements) in the rearranged recombinase vectors were confirmed by sequencing. We also show that an Alu element in the T-cell receptor α chain gene may act as RSSs. Alu sequences are frequently found in introns and 3' untranslated regions of genes. This study may shed some light on the source of the heterogeneous rearrangements in lymphocytic leukemias. In addition, recombinations at these Alu sequences provide the potential for the formation of fusion proteins and exchanges of promoter elements between genes. Work performed under auspices of the US DOE by the Lawrence Livermore National Laboratory; contract No. W-7405-ENG-48